advance the prosecution of this case, Applicants have canceled, without prejudice, nonelected claims 2, 7, 8, and 10-25. However, in light of the finality of this Restriction Requirement, Applicants reserve the right to file a divisional application to the canceled subject matter.

II. Information Disclosure Statement

The Examiner has indicated that references AB, AD-AF and AN-AP of the Information Disclosure Statement were not found in the instant application. As indicated in the transmittal sheet forwarded with the IDS, references AB, AE, AN, AO and AP were not provided with the Information Disclosure Statement. These references are standard reference texts cited in the application for their teachings of general procedures known to those of skill in the art. It is Applicants' belief that the United States Patent Office has access to these standard reference texts and due to the voluminous nature, copies are not being provided. Further, these general teachings of procedures do not affect the novelty or unobviousness of the instant claimed invention.

With respect to references AD and AF, Applicants believe that copies were provided with the IDS submitted September 20, 2001. However, Applicants are providing herewith additional copies of references AD and AF for consideration by the Examiner.

III. Rejection of Claims 1, 3-6 and 9 under 35 U.S.C. § 112, first paragraph

Claims 1, 3-6 and 9 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, the Examiner suggests that the specification does not evidence the intended use of SEQ ID NO:8 nor fragment and variant sequences. The Examiner suggests that Applicants have not provided disclosure enabling the use of degenerate coding sequences of SEQ ID NO:8 nor disclosure designating what changes could be tolerated enabling one of ordinary skill in the art to make and use these sequences in any diagnostic method. Further, the Examiner suggests that Applicants have not set forth any supporting evidence that suggests that SEQ ID NO:8 is a unique tumor or molecular marker for colon cancer.

Accordingly, in an earnest effort to advance the prosecution of this case, and without conceding the correctness of the Examiner's position, Applicants have amended claim 1 to delete reference to variant sequences.

Further, Applicants point the Examiner to Example 1 wherein

SEQ ID NO:8 was discovered as being differentially expressed in colon cancer by total mRNA subtractions. Subtractions were performed using colon cancer tissue (tester) and matched normal adjacent colon tissue (driver). Additionally, subtractions were performed using mixtures of non-cancerous, non-colon tissue types as the driver. See page 52, line 5, through page 53, line 27 of the instant application. These combined subtraction approaches identify transcripts that are differentially expressed in colon cancer versus normal colon tissue, and specific or unregulated in colon cancer versus other normal tissues. Accordingly, the source of SEQ ID NO:8 provides additional supporting evidence that SEQ ID NO:8 is useful as a unique marker for colon cancer.

Moreover, Applicants are providing herewith a 37 C.F.R. § 1.132 Declaration by co-inventor Dr. Roberto Macina providing confirming data generated in accordance with teachings of the specification demonstrating that SEQ ID NO:8 is a unique marker for colon cancer. Specifically, Dr. Macina's Declaration provides data from experiments measuring relative levels of SEQ ID NO:8, in cancerous, normal adjacent and normal tissue via quantitative PCR (See paragraphs 4 and 5 of Dr. Macina's Declaration). Procedures for quantitative PCR are described in detail in the instant specification at page 22, line 16-24, page

40, lines 1-14 and page 41, lines 14-31 (also see paragraph 5 of Dr. Macina's Declaration). As shown in the graphs attached to Dr. Macina's Declaration, also summarized in paragraph 6 of Dr. Macina's Declaration, levels of SEQ ID NO:8 are higher in cancer samples when compared to normal tissue and normal adjacent tissue for colon cancer. Further, as discussed in paragraph 7 of Dr. Macina's Declaration, the specificity and sensitivity of SEQ ID NO:8 for colon cancer is at least as high as other markers currently approved and used for diagnosis of various cancers. Accordingly, these data, generated in accordance with teachings provided in the instant specification, provide additional supporting evidence that SEQ ID NO:8 is useful as a unique marker for colon cancer.

Since the executed version of Dr. Macina's Declaration is a facsimile copy, Applicants are also providing an unexecusted courtesy copy of Dr. Macina's Declaration with colored graphs attached.

Withdrawal of this rejection under 35 U.S.C. § 112, first paragraph, is therefore respectfully requested.

IV. Rejection of Claims 1, 5, 6 and 9 under 35 U.S.C. § 112, second paragraph

Claims 1, 5, 6 and 9 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner suggests that the recitation of "hybridizing under stringent conditions" in claim 1 is vague and indefinite. Further the Examiner suggests that the recitation of "CSG" in claims 5, 6 and 9 is indefinite.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended claims 5, 6 and 9 to define the abbreviation CSG as colon specific gene. Support for this amendment can be found throughout the specification and in particular at page 3, lines 16-20 and page 5, lines 16-19.

With respect to the suggested indefiniteness of the recitation of "hybridizing under stringent conditions", Applicants respectfully disagree with the Examiner.

In accordance with MPEP § 2173, the primary purpose of the requirement of definiteness of claim language is to ensure that the scope of the claimed is clear so that the public is informed of the boundaries of what constitutes infringement of the patent.

Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

(A) The content of the particular application disclosure;

(B) The teachings of the prior art; and

(C) The claim interpretation that would be given by one possessing the ordinary level of skill in that pertinent art at the time the invention was made. Only a reasonable degree of particularly and distinctness is required. MPEP § 2173.01. Further, the MPEP and the case law are clear; when reviewing a claim for compliance with 35 U.S.C. § 112, second paragraph, the Examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. § 112, second paragraph.

Part (a) of claim 1 of the instant application is drawn to an isolated polynucleotide comprising a selected SEQ ID NO and part (c) of claim 1, as amended, is drawn to a polynucleotide which hybridizes under stringent conditions an antisense of one of those selected SEQ ID NOs.

Methods for assessing whether a polynucleotide hybridizes under stringent conditions to a selected polynucleotide sequence are well known to those of skill in the art and set forth in

great detail in standard reference texts such as Sambrook et al. 1989 (Molecular Cloning, A Laboratory Manual, 2nd Edition, Cold Spring Harbor Press, Cold Spring Harbor). Such methods can be performed routinely by those of skill in the art to assess whether or not a polynucleotide hybridizes under stringent conditions to, for example SEQ ID NO:8 and thus falls within the scope of the claimed polynucleotides.

Further, the specification at page 18 teaches that by stringent conditions it is meant that hybridization will occur only if there is at least 95%, and more preferably at least 97% identity between the sequences. Accordingly, one of skill in the art can also routinely assess whether or not a polynucleotide falls within the scope of the present invention by determining whether the sequence has 95% or greater identity with a selected SEQ ID NO.

Thus, the claims, as amended are definite when read in light of the teachings of the specification and what is well known by those of skill in the art. Further, the claims when read as a whole apprise one of ordinary skill in the art of their scope, thus meeting the requirements of 35 U.S.C. § 112, second paragraph.

Withdrawal of this rejection under 35 U.S.C. § 112, second

paragraph is therefore respectfully requested.

V. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

Respectfully submitted,

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Date: **January 13, 2003**

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Please cancel claims 2, 7, 8, and 10-25, without prejudice.

Please amend the claims as follows:

1. (amended) An isolated polynucleotide comprising:

(a) SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56 or 57;

(b) a fragment of at least 15 contiguous nucleobases of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56 or 57,

~~(c) a nucleic acid sequence which, due to degeneracy in genetic coding, comprises variations in nucleotide sequence as compared to SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56 or 57, but which still encodes the same protein,~~ or

~~(d)~~ (c) a nucleic acid sequence which hybridizes under stringent conditions to an antisense sequence of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56 or 57.

5. (amended) A method for producing a ~~CSG~~ polypeptide of a

colon specific gene comprising culturing the host cell of claim 4 under conditions which promote expression of the polynucleotide and isolating polypeptide expressed in the cells.

6. (amended) A method for producing a cell expressing a ~~esg~~ polypeptide of a colon specific gene comprising transforming or transfecting a cell with the vector of claim 3 so that the cell, under appropriate culture conditions, expresses a ~~esg~~ polypeptide of a colon specific gene.

9. (amended) A ~~esg~~ colon specific gene for diagnosing colon cancer comprising a polynucleotide of claim 1 or a polypeptide encoded thereby.